Treatment strategies in colorectal cancer patients with initially unresectable liver-only metastases. CAIRO5 a randomized phase 3 study of the Dutch Colorectal Cancer Group (DCCG)

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To determine the median progression-free survival (PFS) and R0/1 secondary resection rate upon induction systemic treatment in colorectal cancer patients with initially unresectable liver-only metastases, stratified by RAS and BRAF tumor mutation...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54605

Source
ToetsingOnline

Brief title
CAIRO5

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
Bowel Cancer, Colorectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Dutch Colorectal Cancer Group
Source(s) of monetary or material Support: Amgen,Dutch Colorectal Cancer Group,Roche Registration Roche Registration GmbH (RRG), Grenzach, Germany

Intervention

Keyword: anti-EGFR, chemotherapy, colorectal cancer, resectability

Outcome measures

Primary outcome

Progression free survival (PFS).

Secondary outcome

- R0/1 resection rate

- Median overall survival

- 3- and 5-year overall survival rates

- Tumor response rate

- Toxicity

- Pathological complete response rate (pCR) of resected lesions

- Postoperative morbidity.

Study description

Background summary

Colorectal cancer patients with initially unresectable liver-only metastases may be cured after downsizing of metastases by induction systemic therapy. However, the optimal induction regimen has not been defined, and no consensus exist on criteria for resectability.

Study objective

To determine the median progression-free survival (PFS) and R0/1 secondary

resection rate upon induction systemic treatment in colorectal cancer patients with initially unresectable liver-only metastases, stratified by RAS and BRAF tumor mutation status and location.

Study design

Colorectal cancer patients with initially unresectable liver-only metastases, as prospectively confirmed by an expert panel according to predefined criteria, will be tested for RAS and BRAF tumor mutation status. Patients with RAS or BRAF mutant tumors and right-sided localised tumors will be randomised between doublet chemotherapy (FOLFOX or FOLFIRI) plus bevacizumab (schedule 1), and triple chemotherapy (FOLFOXIRI) plus bevacizumab (schedule 2). Patients with RAS and BRAF wildtype and left-sided localised tumors will be randomized between doublet chemotherapy (FOLFOX or FOLFIRI) plus either bevacizumab (schedule 1) or panitumumab (schedule 3).

Patient imaging will be reviewed for resectability by a central panel, consisting of at least one radiologist and three surgeons every assessment. Central panel review will be performed prior to randomization as well as during treatment, as described in the protocol.

Intervention

*Schedule 1: 5-fluorouracil, oxaliplatin (FOLFOX) or 5-fluorouracil, irinotecan (FOLFIRI), both combined with bevacizumab
*Schedule 2: 5-fluorouracil, oxaliplatin, irinotecan (FOLFOXIRI) and bevacizumab
*Schedule 3: FOLFOX or FOLFIRI, both combined with panitumumab

Study burden and risks

- Chemotherapy cycles of 2 weeks
- Every 8 weeks CT scan
- All studies will be perfomed on tissue that has already been obtained from patients for diagnostic purposes. No tissue will be collected with the sole purpose of research.

Contacts

Public
Dutch Colorectal Cancer Group

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Den Haag 2595 AR
NL

Scientific
Dutch Colorectal Cancer Group

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Histologically proven colorectal cancer , - unresectable metastases confined to the liver according to CT scan, obtained <= 2 weeks prior to registration. Unresectability will be confirmed by the panel. Patients with small (<= 1 cm) extrahepatic lesions that are not clearly suspicious of metastases are eligible., - RAS/BRAF mutation status known, - WHO performance status 0-1 (Karnofsky performance status >= 70), - Age >= 18 years, - No contraindications for liver surgery, - In case of primary tumor in situ: tumor should be resectable
- In case of resected primary tumor: adequate recovery from surgery, - Adequate organ functions, as determined by normal bone marrow function (Hb ³ 6.0 mmol/L, absolute neutrophil count ³ 1.5 x 109/L, platelets ³ 100 x 109/L), renal function (serum creatinine <= 1.5x ULN and creatinine clearance, Cockroft formula, ³ 30 ml/min), liver function (serum bilirubin <= 2 x ULN, serum transaminases <= 5x ULN), - Life expectancy 12 weeks or more, - Expected adequacy of follow-up, - Written informed consent

Exclusion criteria

- Extrahepatic metastases, with the exception of small (<= 1 cm) extrahepatic lesions that are not clearly suspicious for metastases , - Unresectable primary

tumor, or resectable tumor requiring immediate surgery, - Serious comorbidity or any other condition preventing the safe administration of study treatment (including both systemic treatment and surgery), - Major cardiovascular events (myocardial infarction, severe/unstable angina, congestive heart failure, CVA) within 12 months before registration, - Uncontrolled hypertension, or unsatisfactory blood pressure control with >=3 antihypertensive drugs, - Previous systemic treatment for metastatic disease; previous adjuvant treatment is allowed if completed >= 6 months prior to registration, - Previous surgery for metastatic disease, - Previous intolerance of study drugs in the adjuvant setting, - Pregnant or lactating women, - Second primary malignancy within the past 5 years with the exception of adequately treated in situ carcinoma of any organ or basal cell carcinoma of the skin

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-10-2014
Enrollment:	584
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	CAMPTO
Generic name:	Irinotecan
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Fluorouracil
Generic name:	5-Fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Leucovorin
Generic name:	calciumfolinaat - pentahydraat
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vectibix
Generic name:	Panitumumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-02-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	05-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	20-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	28-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	31-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO

Date:	08-09-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO

Date:	24-01-2025
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-005435-24-NL
ClinicalTrials.gov	NCT02162563
CCMO	NL47650.018.14